Surgical Nerve Decompression at Lower Extremity for Diabetic Neuropathy: A Systematic Review and Meta-Analysis of Time-Dependent Pain, Sensory Recovery, Amputation, Ulcer Recurrence, and Balance

Shahin Naghizadeh[1,2], Maryam Zohrabi-Fard[2], Amir-Ahmad Keramati[2], Alireza Zali[2], Kaveh Oraii Yazdani[3], Sadra Rohani[2], Saeed Oraee-Yazdani[2]

Key words
- Diabetic foot
- Diabetic neuropathy
- Nerve decompression
- Pain management
- Sensory recovery

Abbreviations and Acronyms
2-PD: 2-point discrimination
CI: Confidence interval
DPN: Diabetic peripheral neuropathy
OR: Odds ratio
RCT: Randomized controlled trial
SMD: Standardized mean difference

From the [1]Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [2]Functional Neurosurgery Research Center, Research Institute of Functional Neurosurgery, Shohada Tajrish Neurosurgical Center of Excellence, Shahid Beheshti University of Medical Sciences, Tehran, Iran; and [3]Zahedan University of Medical Sciences, Zahedan, Iran

To whom correspondence should be addressed: Saeed Oraee-Yazdani, M.D., Ph.D. [E-mail: Saeed.o.yazdani@gmail.com]

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OBJECTIVE: **This systematic review and meta-analysis evaluated the efficacy of surgical nerve decompression in patients with diabetic peripheral neuropathy, focusing on pain relief over time, comprehensive sensory function, reduction in ulcer recurrence, amputation prevention, and balance improvement.**

METHODS: **Databases including PubMed, Scopus, and Web of Science were systematically searched up to January 8, 2025. Eighteen studies (4 randomized controlled trials and 14 observational studies; total n = 837) met inclusion criteria. Primary outcomes were pain relief and sensory recovery; secondary outcomes were ulcer recurrence, amputation rates, and balance. Data synthesis employed random-effects or fixed-effects models with heterogeneity and publication bias assessments.**

RESULTS: **Surgical decompression significantly reduced pain at short-term (6 months: standardized mean difference [SMD]: 2.40, $P < 0.001$), medium-term (12 months: SMD: 2.02, $P = 0.014$), and long-term (> 12 months: SMD: 3.24, $P = 0.009$) follow-ups. Meta-regression revealed modest attenuation of pain relief over time ($R^2 = 33.1\%$). Continuous measures indicated significant sensory improvements (SMD: 2.19, $P = 0.012$), although categorical controlled comparisons were inconclusive. Surgical intervention significantly reduced ulcer recurrence (log odds ratio: 1.03, $P < 0.001$) and amputation rates (log odds ratio: 2.06, $P = 0.018$), while improvements in balance showed a positive, yet nonsignificant, trend.**

CONCLUSIONS: **Surgical nerve decompression demonstrates sustained efficacy in pain management and substantially reduces severe diabetic neuropathy complications. Future high-quality randomized controlled trials are necessary to standardize outcomes and confirm long-term benefits.**

INTRODUCTION

Diabetes mellitus remains a global health challenge, affecting 366 million people in 2011, and projected to rise to 552 million by 2030, with more recent research suggesting these numbers are conservative.[1] Diabetic peripheral neuropathy (DPN), which affects an estimated 30% of patients with diabetes, and its prevalence increases with disease duration.[2,3] DPN is characterized by sensory and motor dysfunction attributable to diabetes in the absence of other peripheral neuropathy causes.[4,5] Clinically, patients often report itching, burning, numbness, tingling, paresthesia, and pain, particularly in the lower extremities.[6-10] When motor nerves are involved, muscle atrophy and foot muscle imbalance can lead to heightened fall risk, ataxia, foot ulceration, gangrene, and eventual amputation, all of which adversely impact quality of life.[6-10]

Because the natural history of DPN is generally "progressive and irreversible",[11] strategies for tight glucose control have shown conflicting results in preventing its onset.[12,13] Standard medical therapies often relieve pain without halting disease progression.[14] Consequently, surgical approaches—especially nerve decompression based on the concept of double crush syndrome—have garnered increased interest. According to this concept, impaired axoplasmic flow ("first crush") in peripheral nerves is exacerbated by anatomical compressions ("second crush").[13] In line with this idea, Dellon introduced peripheral nerve decompression as a surgical option for symptomatic neuropathy.[14]

Despite 3 decades of investigation into surgical decompression for DPN, systematic reviews have repeatedly assigned the evidence a class IV rating, citing limited study design quality and categorizing this approach as "unproven" rather than "ineffective".[15] Clinicians thus face uncertainty in recommending nerve

decompression as part of standard care. Moreover, a previous meta-analysis by Fadel et al.[16] did not examine the effect of time on outcomes and restricted its sensory recovery assessment to 2-point discrimination (2-PD), leaving other critical sensory metrics unaddressed. Additionally, Fadel's review did not evaluate the impact of nerve decompression on balance, an important functional parameter in patients with DPN.

Against this backdrop, we conducted a systematic review and meta-analysis to comprehensively evaluate nerve decompression surgery in DPNs. First, we sought to determine whether the effectiveness of nerve decompression diminishes over time, thus exploring a limitation of Fadel's review. We also expanded the sensory recovery domain beyond 2-PD to include all reported and assessable sensory outcomes and, for the first time in a meta-analysis, assessed balance improvement as a potential benefit of surgical intervention. Finally, we investigated whether the potential decline in effectiveness pattern differs between observational studies and randomized controlled trials (RCTs). Due to data constraints, we could only examine time-dependent effects in the pain domain, a limitation that underscores the persistent need for rigorous and consistent reporting of outcomes in this field.

METHODS

Protocol and Eligibility Criteria

This systematic review and meta-analysis was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analysis guidelines.[17] The inclusion criteria focused on adults with DPN who underwent surgical decompression of peripheral nerves in the lower extremities. Comparators included either the contralateral nonoperated limb or patients with DPN treated without surgery. Primary outcomes included postoperative pain improvements (assessed via visual analog scale) and sensory function; secondary outcomes included ulcer recurrence, amputation rates, and balance improvement. Studies were excluded if they involved pre-existing compression neuropathies unrelated to DPN, animal or in vitro research, reviews, expert opinions, case reports, or non-English articles.

Search Strategy and Study Selection

A comprehensive search was performed across Scopus, PubMed, and Web of Science from their inception to January 8, 2025, using key terms such as "Diabetic Neuropathies," "Diabetic Peripheral Neuropathy," "surgical decompression," "nerve decompression," and "treatment outcome." Only studies published in English and involving human subjects were included. After removing duplicates, 2 reviewers (M. Z. and A. K.) independently screened all titles and abstracts. Those deemed potentially eligible underwent full-text evaluation, and final inclusion was determined with input from a third reviewer (S. N.).

Data Extraction

Data extraction was independently conducted by M. Z. and A. K., with oversight by S. N. Information gathered included author names, publication year, study design, population characteristics, surgical intervention details, follow-up duration, and measured outcomes. Quality assessments were performed using the Cochrane Risk of Bias 2 tool for RCTs and the Risk of Bias in Nonrandomized Studies of Interventions for cohort studies. No study was excluded based on the risk of bias scores.

Statistical Analysis

Statistical analyses were conducted using Comprehensive Meta-Analysis version 3.0 and Statistical Package for the Social Sciences version 29 (IBM Corp., Armonk, NY), with a significance threshold of $P < 0.05$. Pain outcomes were expressed as standardized mean differences with Hedges' g. Sensory recovery data were categorized into continuous (Hedges' g), binary (log odds ratio [OR]), or proportional (logit event ratio) formats based on how each study reported results. Log OR was used for ulcer recurrence and amputation risk, while logit event ratio was employed for balance outcomes. Heterogeneity was assessed using the Cochrane Q (χ^2) and I^2 statistics; if $I^2 < 25\%$ and $P > 0.05$, a fixed-effects model was applied; otherwise, a random-effects model was used. Publication bias was evaluated using Egger's regression asymmetry test and funnel-plot inspection, supplemented by the trim-and-fill method if indicated. Subgroup analyses and meta-regression were performed to identify sources of heterogeneity, including study design and follow-up duration. Notably, because of insufficient longitudinal data in most outcome domains, time-dependent effects could only be thoroughly investigated for pain outcomes.

RESULTS

Included Studies

An initial database search yielded 831 records, of which 552 remained after duplicate removal (Figure 1). Following title and abstract screening, 500 studies were excluded for not meeting inclusion criteria, leaving 52 for full-text review. Following detailed evaluation, 34 studies were excluded for the following reasons: 1 study was removed due to a duplicate report,[5] 1 study was excluded for using simulation-based methods,[18] 14 studies did not report the relevant data or outcomes required for the analysis,[7,14,19-29] 2 studies were in non-English languages without accessible translations,[30,31] and 10 studies were review articles from which primary data could not be extracted.[32-41] Six additional reports were retrieved but excluded from the final analysis due to noncompatible data for extraction.[3,9,42-45] Ultimately, 18 studies were included in the final analysis (4 RCTs and 14 observational studies), encompassing 837 patients. Of these 7 examined pain,[4,6,46-50] 8 addressed sensory recovery,[47,49,51-56] 4 analyzed ulcer recurrence,[11,15,57-59] 3 investigated amputation,[11,15,58] and 2 reported on balance improvements.[53,54] Full study characteristics are summarized in Tables 1–4.

Risk of Bias and Quality Assessment

The summarized results of the risk of bias assessments for both RCTs and cohort studies are presented in Figure 2 (Panels A and B, respectively).

Primary Outcomes

Pain. *Short-Term Follow-Up (6 Months).* Seven studies[4,6,46-50] evaluated pain outcomes at short-term (6 months), medium-term (12 months), and long-term

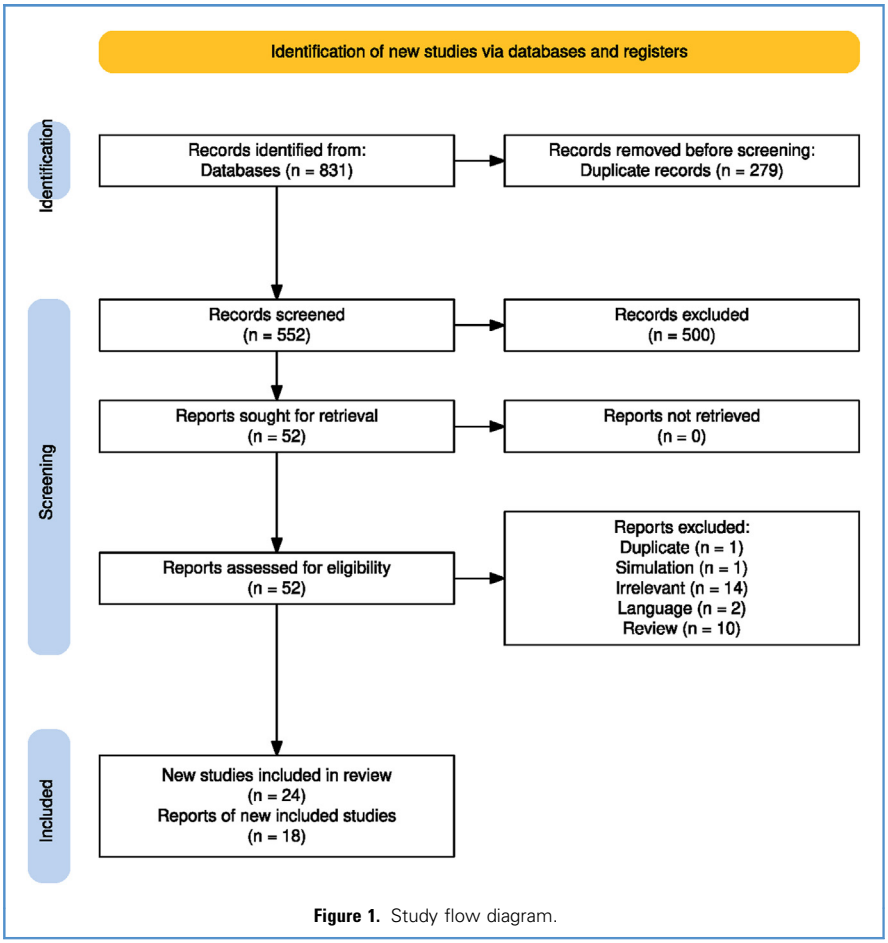


Figure 1. Study flow diagram.

(> 12 months) follow-up periods using random-effects models and subgroup analyses by study design. At 6 months, the pooled effect size was −2.40 (95% confidence interval [CI]: −3.22 to 1.57, $P < 0.001$), indicating a significant reduction in pain. Subgroup analysis demonstrated similar improvements in both RCTs (−2.58, 95% CI: −2.89 to 2.28, $P < 0.001$) and observational studies (−2.29, 95% CI: −4.21 to 0.39, $P = 0.032$). However, heterogeneity was substantial ($I^2 = 83.3\%$), primarily driven by observational studies ($I^2 = 90.4\%$) (Figure 3A).

Medium-Term Follow-Up (12 Months). At 12 months, the overall pooled effect size was −2.02 (95% CI: −3.26 to 0.78, $P = 0.014$), reflecting continued pain relief. Observational studies showed a stronger effect (−2.52, 95% CI: −3.23 to 1.81, $P = 0.014$) compared to RCTs (−1.56, 95% CI: −9.63 to 6.51, not significant). Heterogeneity was moderate ($I^2 = 71.4\%$), pointing to study variability (Figure 3B).

Long-Term Follow-Up (> 12 Months). Long-term follow-up (> 12 months) revealed a more pronounced pooled effect size of −3.24 (95% CI: −4.91 to 1.56, $P = 0.009$). Both RCTs (−4.16, 95% CI: −6.38 to 1.94, $P = 0.027$) and observational studies (−2.36, 95% CI: −3.25 to 1.46, $P = 0.019$) maintained significant reductions in pain, although subgroup differences were statistically significant ($P = 0.003$), with RCTs yielding larger effect sizes. Residual heterogeneity remained moderate ($I^2 = 66.8\%$) (Figure 3C).

Meta-Regression. A meta-regression analysis examined the influence of follow-up duration on treatment effectiveness, identifying a significant negative association between time and effect size ($F = 9.289$, $P = 0.008$). Pain reduction thus appears to diminish somewhat over extended follow-up, and although follow-up duration explained 33.1% of the variance in effect sizes ($R^2 = 33.1\%$), residual heterogeneity remained high ($I^2 = 69.4\%$, $\tau^2 = 0.407$). This suggests that additional moderators may contribute to variability (Figure 3D). These factors might include differences in glycemic control and patient adherence to postoperative care. Nevertheless, pain reductions remained statistically significant at each time point, highlighting surgical nerve decompression as a valuable long-term option for mitigating neuropathic pain when conservative measures fail.

Sensory Recovery. By examining a range of sensory measures, this meta-analysis expands upon prior reviews that narrowly focused on 2-PD. We incorporated data from studies reporting diverse sensory outcomes and analyzed them in 3 distinct groups: continuous studies, categorical studies without a control group, and categorical studies with a control group.

Group 1: Continuous Studies. Three continuous studies[47,49,56] showed a significant pooled effect size of −2.19 (95% CI: −3.21 to 1.17, $P = 0.012$), indicating substantial improvements in sensory function. Subgroup analysis revealed that observational studies without a control group had an effect size of −2.16 (95% CI: −7.16 to 2.83, $P = 0.114$), whereas the single included RCT with a control group (−2.34) could not be statistically evaluated due to limited data. Overall heterogeneity was low ($I^2 = 30.4\%$, $\tau^2 = 0.057$), although observational studies alone demonstrated moderate heterogeneity ($I^2 = 58.2\%$, $\tau^2 = 0.184$). Publication bias testing using trim-and-fill identified 2 imputed studies, adjusting the pooled effect size to −1.83 (95% CI: −2.63 to 1.03, $P = 0.003$), suggesting the findings are robust despite possible bias (Figure 4A).

Group 2: Categorical Studies without a Control Group. In 3 studies[53-55] in the categorical studies lacking a control group, the pooled logit event ratio was 1.66 (95% CI: 0.14 to 3.17, $P = 0.042$), signifying a significant increase in the proportion of patients reporting improved sensory function postintervention. Heterogeneity was moderate ($I^2 = 60.3\%$, $\tau^2 = 0.191$), but this variation was not statistically

Table 1. Summary of the Randomized Controlled Trials Included in This Review

Authors	Year of Publication	Title	Country	Study Design	Outcomes
Rozen et al.	2024	Effect of Lower Extremity Nerve Decompression in Patients With Painful Diabetic Peripheral Neuropathy: The Diabetic Neuropathy Nerve Decompression Randomized, Observation Group and Placebo Surgery-Controlled Clinical Trial	USA	Randomized controlled trial	Pain
Ma, F. et al.	2023	Improving Effects of Peripheral Nerve Decompression Microsurgery of Lower Limbs in Patients with Diabetic Peripheral Neuropathy	China	Randomized controlled trial	Pain and sensory recovery
Mahmoud et al.	2022	Tibial Nerve Decompression in The Tarsal Tunnel versus Conservative Measures in The Treatment of Painful Diabetic Polyneuropathy	Egypt	Randomized controlled trial	Ulcer recurrence
Maurik et al.	2014	Value of surgical decompression of compressed nerves in the lower extremity in patients with painful diabetic neuropathy: a randomized controlled trial	Netherland	Randomized controlled trial	Sensory recovery

significant (Q = 4.69, df = 2, P = 0.096). No studies were imputed by trim-and-fill analysis, reinforcing the stability of the observed effect size (Figure 4B).

Group 3: Categorical Studies with a Control Group. Two studies[51,52] are categorical and included a control group; the pooled log OR was 0.90 (95% CI: 7.91 to 9.70, P = 0.418), indicating no significant difference when comparing intervention and control arms. A subgroup analysis found a notable positive effect in 1 observational study by Rinkel et al.[51] (log OR: 1.63, 95% CI: 0.07 to 3.20, P = 0.041), whereas the RCT by van Maurik et al.[52] showed a nonsignificant result (0.25, 95% CI: 1.17 to 1.66, P = 0.734). Heterogeneity was low to moderate (I^2 = 39.9%, τ^2 = 0.385), suggesting that variability between these studies might be due to chance (Figure 4C).

Secondary Outcomes

Amputations. Three studies[11,15,58] assessed amputation rates using a fixed-effects model, yielding a pooled effect size of −2.06 (95% CI: −3.77 to 0.35, P = 0.018). Although individual results did not all reach statistical significance, they consistently trended toward fewer amputations in the surgical group. Notably, heterogeneity was absent (I^2 = 0%), indicating strong consistency across settings and study designs. Publication bias assessments, including trim-and-fill and Egger's regression test, detected no evidence of bias, and the pooled effect size remained unchanged. These findings support the reliability of the observed risk reduction in amputation (Figure 5A).

Ulcer Recurrence. Five studies (1 RCT and 4 observational) reported on ulcer recurrence.[11,15,57-59] The fixed-effects pooled effect size was −1.032 (95% CI: −1.557 to 0.507, P < 0.001), suggesting a significant decrease in ulcer formation following nerve decompression. Low heterogeneity (I^2 = 16.1%, P = 0.31) reinforced the appropriateness of a fixed-effects approach, and publication bias evaluations revealed no indications of asymmetric reporting (Egger's test P = 0.696). Individual effect sizes ranged from −3.219 to 0.405, with the largest single weight (45.8%) contributed by an observational study by Nickerson et al.[15] Despite differences in study design, all 5 studies showed consistent reductions in ulcer recurrence, bolstering confidence in the intervention's effectiveness (Figure 5B).

Balance Improvement. Two studies evaluated balance postintervention via logit event sizes, analyzed with a random-effects model.[53,54] The pooled effect size was 1.876 (95% CI: 4.37 to 8.12, P = 0.163), suggesting a positive but nonsignificant trend toward improved balance after surgical decompression. Heterogeneity was substantial (I^2 = 70.2%, Q = 3.36, df = 1, P = 0.067), indicating possible systematic differences in study populations, measurement tools, or follow-up durations. Given the limited number of studies and notable variability, these preliminary findings warrant caution in interpreting balance improvements and underscore the need for further research with standardized protocols (Figure 5C).

DISCUSSION

This meta-analysis underscores the potential of surgical nerve decompression to improve a variety of clinical outcomes in patients with diabetic neuropathy, addressing several gaps identified in previous reviews. Most notably, the study sheds light on time-dependent pain outcomes, provides a broader perspective on sensory recovery measures, and expands the scope of the investigation to include balance—a domain that has thus far been underexplored.

In these studies, the surgical interventions targeted multiple peripheral nerve entrapments in the lower extremity. The most frequently decompressed nerves were the tibial nerve at the ankle (tarsal tunnel, often including its medial and lateral plantar branches) and the common peroneal (fibular) nerve at the fibular head, followed by the deep peroneal nerve on the dorsum of the foot. Several studies also reported decompression of the superficial peroneal nerve in the lateral compartment of the leg or the proximal tibial nerve at the soleal sling (a fibrous arch in the upper calf) when clinically indicated. Most studies explicitly described using a decompression approach based on Dellon's technique, which involves releasing multiple lower-extremity nerves during the same operation. A few studies focused on a single nerve, but overall, the intervention was relatively consistent across trials. The surgeries were predominantly performed by specialists in neurosurgery or plastic,

Table 2. Summary of the Observational Studies Included in This Review

Authors	Year of Publication	Title	Country	Study Design	Outcomes
Qi Wang et al.	2018	Two-Point Discrimination Predicts Pain Relief after Lower Limb Nerve Decompression for Painful Diabetic Peripheral Neuropathy	China	Retrospective study	Pain
Rinkel et al.	2018	Optimization of Surgical Outcome in Lower Extremity Nerve Decompression Surgery	Netherland	Retrospective study	Sensory recovery
Anderson et al.	2017	Acute Improvement in Intraoperative EMG Following Common Fibular Nerve Decompression in Patients with Symptomatic Diabetic Sensorimotor Peripheral Neuropathy: 1. EMG Results	USA	Retrospective study	Pain
W. Yang et al.	2016	Pain Relief and Health-Related Quality-of-Life Improvement After Microsurgical Decompression of Entrapped Peripheral Nerves in Patients With Painful Diabetic Peripheral Neuropathy	China	Prospective	Pain
Nickerson et al.	2014	Nerve decompression after diabetic foot ulceration may protect against recurrence: a 3-year controlled, prospective analysis	USA	Prospective cohort	Amputation and ulcer recurrence
Valdivia et al.	2013	Surgical treatment of superimposed, lower extremity, peripheral nerve entrapments with diabetic and idiopathic neuropathy	USA	Retrospective study	Balance improvement and sensory recovery
Nickerson et al.	2013	Low long-term risk of foot ulcer recurrence after nerve decompression in a diabetes neuropathy cohort	USA	Retrospective study	Amputation and ulcer recurrence
William et al.	2012	Soleal Sling Syndrome (Proximal Tibial Nerve Compression): Results of Surgical Decompression	USA	Retrospective study	Pain
Nickerson et al.	2010	Low recurrence rate of diabetic foot ulcer after nerve decompression	USA	Retrospective study	Ulcer recurrence
Karagoz et al.	2008	Early and late results of nerve decompression procedures in diabetic neuropathy: a series from Turkiye	Turkiye	Cohort	Pain and sensory recovery
Siemionow et al.	2006	Clinical outcome of peripheral nerve decompression in diabetic and nondiabetic peripheral neuropathy	USA	Retrospective study	Sensory recovery
Valdivia et al.	2005	Surgical treatment of peripheral neuropathy: outcomes from 100 consecutive decompressions	USA	Prospective study	Balance improvement and sensory recovery
Aszmann et al.	2004	Changing the natural history of diabetic neuropathy: incidence of ulcer/amputation in the contralateral limb of patients with a unilateral nerve decompression procedure	USA	Retrospective study	Amputation and ulcer recurrence
Aszmann et al.	2000	Results of decompression of peripheral nerves in diabetics: A prospective, blinded study	USA	Prospective study	Sensory recovery

EMG, electromyography.

with some studies involving orthopedic surgeons, general surgeons, or podiatric surgeons as part of the operative team. Full interventions and surgeons' characteristics are summarized in Tables 3 and 4. This consistency in surgical method and expertise across most studies lends a degree of homogeneity to the intervention despite the diverse study designs and populations.

Primary Outcomes

Pain. The pooled analyses revealed substantial pain reduction after surgical decompression at short-term, medium-term, and long-term follow-up periods, albeit with varying degrees of heterogeneity. At 6 months, the overall effect size was −2.40 (95% CI: −3.22 to 1.57, $P < 0.001$), underscoring a marked initial benefit. RCTs yielded particularly robust effect sizes (e.g., −2.58, 95% CI: −2.89 to 2.28, $P < 0.001$), suggesting that under controlled conditions, surgical decompression consistently reduces neuropathic pain in persons with diabetes populations. Observational studies corroborated this conclusion, albeit with greater variability ($I^2 = 90.4\%$).

In the medium term (12 months), observational studies continued to show significant benefits (pooled effect size: −2.52), whereas the pooled RCT effect size (−1.56) was not statistically significant. This discrepancy may stem from differences in patient selection, methodology, and smaller sample sizes within RCTs. Nonetheless, the overarching trend still supports the efficacy of nerve decompression in reducing pain.

Long-term follow-up analyses (> 12 months) demonstrated a sustained positive effect, with an overall pooled effect size of −3.24 (95% CI: −4.91 to 1.56, $P = 0.009$). Intriguingly, RCTs reported an even stronger effect size (−4.16), highlighting that well-controlled studies can yield especially pronounced pain reductions over extended periods. Despite these findings, significant heterogeneity

Table 3. Demographics of the Randomized Controlled Trials Included in This Review

Authors	Number of Patients	Last Follow-Up	Mean Age	Gender (Male Percentage)	Decompressed Nerves	Surgeon Specialty	Decompression Method
Rozen et al.	78	12	52.5	53.80%	The common peroneal nerve; the deep peroneal nerve; and the tibial, medial, and lateral plantar nerves	Plastic surgeon	N/A
Ma, F. et al.	69 (46)	6	63.8	47.00%	The common peroneal nerve, the deep peroneal nerve, and the tibial nerve	Neurosurgeon	Dellon
Mahmoud et al.	42	6	55.22	28.50%	Posterior tibial nerve branches (medial plantar, lateral plantar, and calcaneal)	General surgery	N/A
Maurik et al.	38	12	62.7	62.70%	Tibial nerve, common peroneal nerve, and deep or superficial nerve	Plastic surgery	Dellon

N/A, not applicable.

persisted (I^2 = 66.8%), likely reflecting varied study protocols, patient populations, and surgical techniques.

The pooled data across short-term (6 months), medium-term (12 months), and long-term (> 12 months) follow-ups reveal consistently significant reductions in neuropathic pain following surgical decompression. Although effect sizes at each time point (−2.40, −2.02, and −3.24, respectively) demonstrate robust clinical improvements, subgroup analyses indicate that heterogeneity remains pronounced, particularly within observational studies. Furthermore, a meta-regression suggested that while pain relief diminishes to some degree over time (R^2 = 33.1%), factors beyond follow-up duration likely contribute to the observed variability. These might include surgical technique differences, glycemic control, and patient adherence to postoperative care protocols. Nevertheless, pain reductions remained statistically significant at each interval, highlighting surgical nerve decompression as a valuable long-term option for mitigating neuropathic pain when conservative measures fail.

Sensory Recovery. By examining a range of sensory measures, this meta-analysis expands upon the prior narrow focus on 2-PD and by providing a comprehensive evaluation of interventions targeting sensory recovery, incorporating data from 3 distinct study designs: continuous studies, categorical studies without a control group, and categorical studies with a control group. The findings highlight the complexities and variability in assessing sensory outcomes across different methodologies.

The pooled effect size of −2.19 (95% CI: −3.21 to 1.17, P = 0.012) for continuous studies underscores significant improvements in sensory function across 3 continuous studies. Subgroup analysis revealed differences between observational studies without a control group (−2.16, 95% CI: −7.16 to 2.83, P = 0.114) and the single RCT with a control group by Ma et al.[47] (−2.34, no statistical evaluation due to limited data). Despite the variability reflected by the wide confidence intervals in observational studies, these findings indicate that both observational and controlled designs support the efficacy of interventions. After adjusting for publication bias using the trim-and-fill method, the pooled effect size was revised to −1.83 (95% CI: −2.63 to 1.03, P = 0.003), reinforcing the robustness of these improvements. Although an RCT in this group offers a valuable reference point for controlled conditions, the inability to statistically assess its results due to limited data highlights the need for more high-quality trials.

In categorical studies without a control group, the pooled logit event ratio was 1.66 (95% CI: 0.14 to 3.17, P = 0.042), indicating a significant increase in the proportion of patients reporting sensory improvement. Moderate heterogeneity (I^2 = 60.3%, τ^2 = 0.191) was observed, but its lack of statistical significance (Q = 4.69, df = 2, P = 0.096) suggests that such variability may be due to chance. Notably, trim-and-fill analysis revealed no imputed studies supporting the stability of these findings. In contrast, categorical studies with a control group yielded a pooled log OR of 0.90 (95% CI: 7.91 to 9.70, P = 0.418), indicating no overall significant difference. Subgroup analysis nevertheless showed a positive effect in 1 observational study by Rinkel et al.[51] (log OR: 1.63, 95% CI: 0.07 to 3.20, P = 0.041), whereas the RCT by Maurik et al.[52] revealed a nonsignificant result (log OR: 0.25, 95% CI: 1.17 to 1.66, P = 0.734). The low-to-moderate heterogeneity (I^2 = 39.9%, τ^2 = 0.385) suggests that differences between these studies could stem from chance-related or design-related factors.

These data suggest that interventions targeting sensory recovery can confer meaningful benefits in observational and uncontrolled settings, as evidenced by the significant improvements found in both continuous and categorical analyses. However, the nonsignificant effect in controlled studies highlights the challenges in translating these findings into definitive clinical recommendations given the potential biases associated with observational research and the stricter methodological constraints of randomized trials. Going forward, high-quality RCTs with standardized, validated sensory assessment tools and larger sample sizes are essential for confirming these effects and reducing heterogeneity. Harmonizing outcome measures across study designs will also facilitate more direct comparisons and strengthen the evidence base for

Table 4. Demographics of the Observational Studies Included in This Review

Authors	Number of Patients	Last Follow-Up	Mean Age	Gender (Male Percentage)	Decompressed Nerves	Surgeon Specialty	Decompression Method
Qi Wang et al.	34	12	56.41	55.88	The common peroneal nerve, the tibial nerve and its branches, and the deep peroneal nerve	Neurosurgeon	Dellon
Rinkel et al.	23	12	61.6	58%	Common peroneal nerve, superficial peroneal nerve, deep peroneal nerve, and tibial nerve	Plastic surgeon	Dellon
Anderson et al.	37	12	64.8	55%	Common fibular nerve	Podiatric surgeon	Dellon
W. Yang et al.	11	12	62.9	54.60%	The common peroneal nerve, posterior tibial nerve, and deep peroneal nerve	Neurosurgeon	Dellon
Nickerson et al.	42	36	74	Not reported	The common peroneal nerve; the dorsal sensory branch of the deep peroneal nerve; and the posterior tibial, medial calcaneal, medial plantar, and lateral plantar branches of the tibial nerve	Plastic, orthopedic, and podiatric surgeons	Dellon
Valdivia et al.	93	12	62	52%	The common peroneal nerve; deep peroneal nerve; tibial nerve and its branches; and the calcaneal, medial plantar, and lateral plantar nerves	Plastic surgeon	Dellon
Nickerson et al.	75	60	74.5	Not reported	The common peroneal nerve; the dorsal sensory branch of the deep peroneal nerve; and the posterior tibial, medial calcaneal, medial plantar, and lateral plantar branches of the tibial nerve	Plastic, orthopedic, and podiatric surgeons	Dellon
William et al.	10	18	67.8	60%	Proximal tibial nerves	Plastic surgeon	Dellon
Nickerson et al.	75	12	74.5	Not reported	The common peroneal nerve; the dorsal sensory branch of the deep peroneal nerve; and the posterior tibial, medial calcaneal, medial plantar, and lateral plantar branches of the tibial nerve	Five surgeons and podiatric physicians	Dellon
Karagoz et al.	24	6	48	Not reported	The posterior tibial nerve and its branches and the common peroneal and the deep peroneal nerve	Plastic surgeon	Dellon
Siemionow et al.	32	7.7	49.55	31	Common peroneal nerve and deep peroneal nerve and tibial nerve	Plastic surgeon	Dellon
Valdivia et al.	39	12	63.1	56%	The common and deep peroneal and tibial nerve	Plastic surgeon	Dellon
Aszmann et al.	50	54	Not reported	Not reported	Tibial and peroneal nerves (deep and common)	Plastic surgeon	Dellon
Aszmann et al.	20	23.3	51.9	25%	The posterior tibial nerve at the ankle and its calcaneal and medial and lateral plantar branches	Plastic surgeon	N/A

N/A, not applicable.

surgical interventions that restore sensory function in diabetic neuropathy.

Secondary Outcomes

Amputations. The pooled analysis of 3 studies demonstrated a statistically significant reduction in amputation risk (effect size: −2.06, P = 0.018), highlighting the potential for nerve decompression to prevent this severe complication. Notably, there was no evidence of heterogeneity (I^2 = 0%) or publication bias, suggesting that the results are both consistent and robust.

Despite the small number of included studies, these findings reinforce the notion that early and effective surgical intervention could avert lower-limb amputations in high-risk persons with diabetes. This protective effect is likely mediated through the preservation of peripheral nerve function in the foot and ankle, resulting in improved pain control, enhanced proprioception, and superior ulcer prevention and wound healing. Collectively, these outcomes may

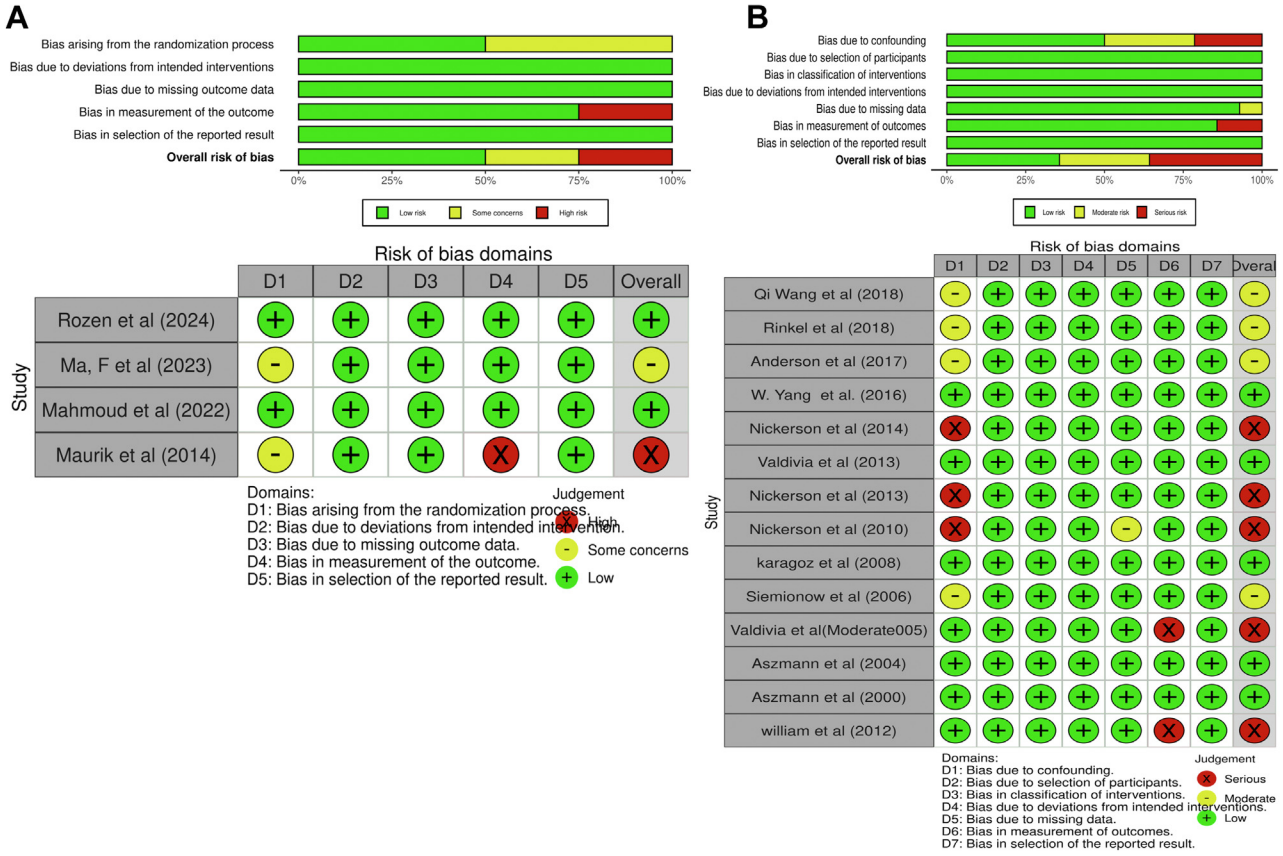


Figure 2. Risk of bias assessment for RCTs and observational studies. Panel **A** shows the ROB-2 assessment for the 4 randomized controlled trials, with the proportion of studies rated as "low risk," "some concerns," or "high risk" in each domain (randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of the reported result). It also provides a study-level summary of the risk of bias judgments across these domains for each RCT. Panel **B** depicts the ROBINS-I evaluation for the cohort studies, highlighting the percentage of observational studies judged to have "low," "moderate," or "serious" risk of bias in each domain (confounding, participant selection, intervention classification, deviations from intended interventions, missing data, outcome measurement, and selection of reported results). A study-by-study breakdown of the risk of bias for each observational study is also presented. RCTs, randomized controlled trials; ROB-2, Risk of Bias 2; ROBINS-I, Risk of Bias in Nonrandomized Studies of Interventions.

substantially reduce the risk of amputation. Future research would benefit from large-scale, multicenter RCTs to further validate these benefits and explore cost-effectiveness analyses that could support broader implementation of nerve decompression.

Ulcer Recurrence. A similarly encouraging outcome was observed in ulcer recurrence, with a pooled effect size of −1.032 (95% CI: −1.557 to 0.507, $P < 0.001$), indicating a notable reduction in ulcer formation among patients who underwent surgical decompression. Low heterogeneity ($I^2 = 16.1\%$) bolstered the reliability of these findings, and neither Egger's test nor trim-and-fill analyses revealed significant publication bias.

Although the data comprised 1 RCT by Mahmoud et al.[57] and 4 observational studies,[11,15,58,59] the consistent reduction in ulcer recurrence across both study types emphasizes the generalizability of these results. Importantly, observational data can complement RCTs by capturing more diverse patient populations and real-world clinical scenarios. From a clinical perspective, the restoration of protective sensation and reduction in neuropathic pain following nerve decompression likely enhance patients' ability to recognize and respond to minor foot trauma, ultimately reducing the risk of ulcer formation. Further studies that standardize outcome measures and use uniform follow-up intervals will help confirm these results and guide clinical practice.

Balance Improvement. The analysis of balance outcomes suggested a positive trend (pooled effect size: 1.876), but this failed to reach statistical significance, and heterogeneity was substantial ($I^2 = 70.2\%$). Only 2 studies met the inclusion criteria. The observed trend may be attributed to improved foot sensation and reduced pain following nerve decompression, leading to enhanced proprioception and greater confidence during ambulation. While these preliminary findings hint at potential benefits for gait stability and fall

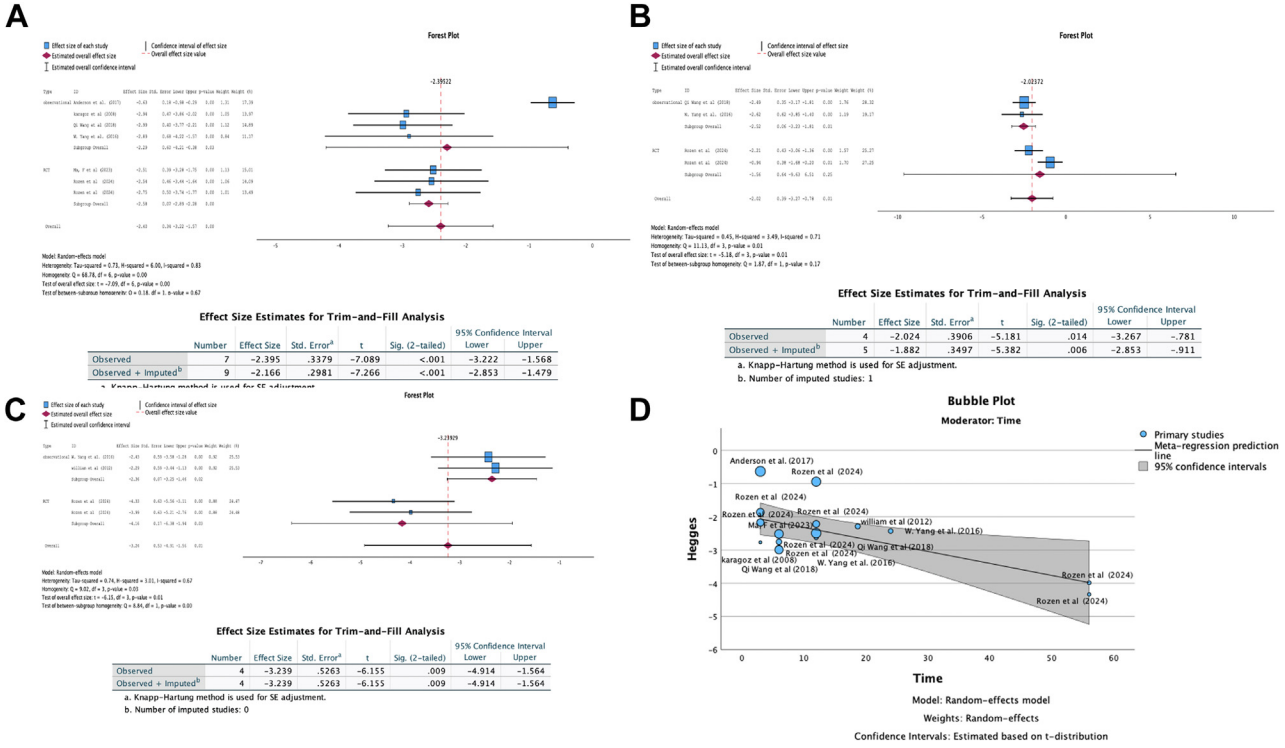


Figure 3. The forest plot and trim-and-fill analysis results (**A**) for short-term follow-up, (**B**) for medium-term follow-up, and (**C**) for long-term follow-up. The forest plot shows the effect size and 95% confidence intervals for individual studies, the overall pooled estimate, and the trim-and-fill analysis results, demonstrating the robustness of the pooled estimate and addressing potential publication bias. (**D**) The meta-regression bubble plot evaluates the effect of the follow-up period (time since intervention) on pain reduction. Random-effects meta-regression with Knapp-Hartung adjustments was used. The regression line illustrates the trend of pain reduction over time, while the shaded area depicts the 95% confidence interval. Bubble sizes correspond to the study weights, with larger bubbles indicating greater influence on the analysis.

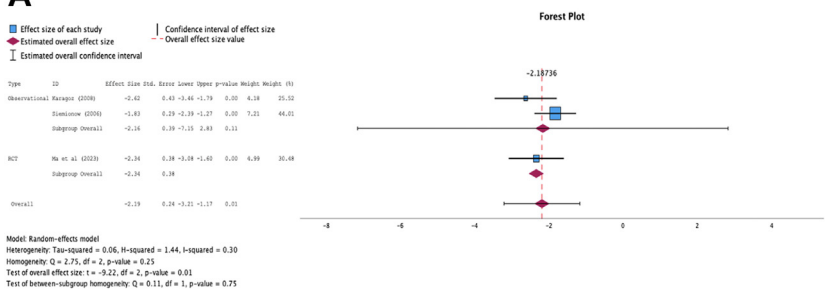
prevention, the limited data and methodological differences underscore the need for larger, more rigorously designed trials with standardized balance measures.

Mechanistically, surgical decompression of peripheral nerves in diabetic neuropathy is thought to confer benefits by alleviating chronic nerve entrapment, thus restoring more normal nerve function. In diabetic limbs with neuropathy, chronically elevated perineural pressures at common entrapment sites, for instance, tarsal tunnel and fibular neck, can impair the nerve's blood supply (vasa nervorum) and disrupt axonal transport (axoplasmic flow). Decompression relieves this pressure, which can improve endoneurial blood flow and re-establish axoplasmic flow within the nerve, facilitating the recovery of axons and myelin. As a result, nerve conductivity and function may improve, leading to reductions in neuropathic pain and partial restoration of sensation. Over time, improved sensory and motor nerve function can contribute to secondary benefits such as lower ulceration risk due to regained protective sensation and better balance and gait stability due to improved proprioception. However, definitive evidence for the latter remains limited. These proposed mechanisms align with the double crush hypothesis in DPN, wherein relieving the superimposed compression ("second crush") allows a nerve already vulnerable from diabetes ("first crush") to function more effectively. The surgery removes significant extrinsic stress on the nerves, creating an environment conducive to nerve regeneration and functional recovery.[13]

Strengths and Limitations

A significant strength of this meta-analysis lies in its broad scope, encompassing multiple outcomes and various study designs (RCTs and observational studies), thus offering a more comprehensive understanding of nerve decompression. By examining short-term, medium-term, and long-term follow-up data, this review provides insights into the durability of the intervention's effects, revealing that although pain reduction appears to diminish somewhat over time, significant benefits can be maintained for more than a year.

Nevertheless, residual heterogeneity was noted across nearly all outcomes, pointing to unmeasured confounders such as glycemic control, variations in surgical technique, and patient selection criteria. Moreover, although formal analyses did not suggest a significant influence, publication bias could not be entirely ruled out. The paucity of standardized measurement tools for key outcomes—particularly sensory recovery and balance—poses an additional challenge, as does the relatively small number of studies contributing long-term data in domains beyond pain. Future research efforts should strive to use

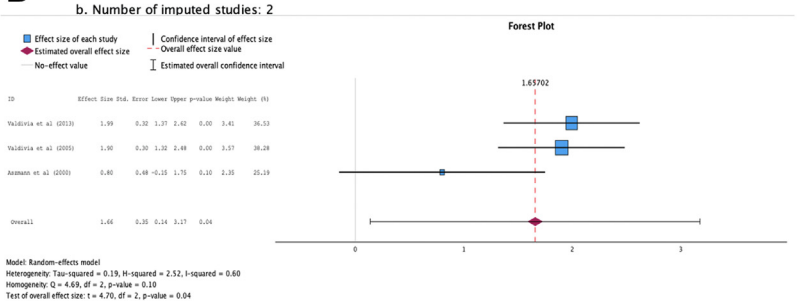


Effect Size Estimates for Trim-and-Fill Analysis

	Number	Effect Size	Std. Error[a]	t	Sig. (2-tailed)	95% Confidence Interval Lower	Upper
Observed	3	-2.187	.2372	-9.222	.012	-3.208	-1.167
Observed + Imputed[b]	5	-1.828	.2894	-6.318	.003	-2.632	-1.025

B

a. Knapp-Hartung method is used for SE adjustment.
b. Number of imputed studies: 2



Effect Size Estimates for Trim-and-Fill Analysis

	Number	Effect Size	Std. Error[a]	t	Sig. (2-tailed)	95% Confidence Interval Lower	Upper
Observed	3	1.657	.3528	4.697	.042	.139	3.175
Observed + Imputed[b]	3	1.657	.3528	4.697	.042	.139	3.175

C

a. Knapp-Hartung method is used for SE adjustment.
b. Number of imputed studies: 0

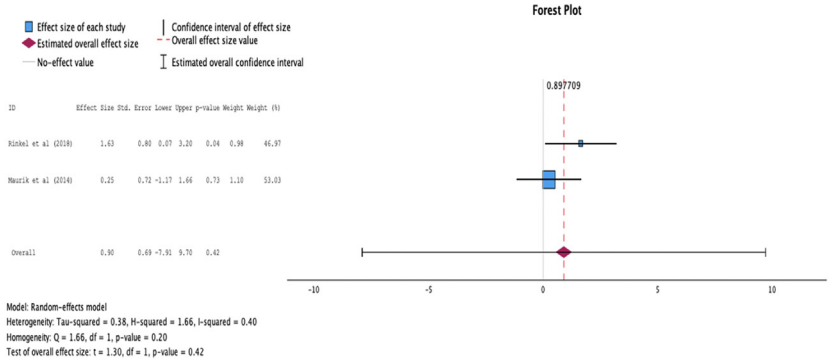


Figure 4. The forest plot and trim-and-fill analysis results (**A**) for continuous studies without a control group, (**B**) for categorical studies without a control group, and (**C**) for categorical studies with a control group. The forest plot, showing the effect size and 95% confidence intervals for individual studies and the overall pooled estimate, and the trim-and-fill analysis results, demonstrating the robustness of the pooled estimate and addressing potential publication bias for categorical studies with a control group; the regression-based test cannot be computed when the number of studies is less than or equal to 3.

consistent, validated measurement instruments and clearly report key statistical metrics (e.g., means, standard deviations) to support more rigorous meta-analyses.

Several potentially informative studies could not be included due to incomplete data reporting, lack of standard deviations, or incompatible outcome measures. This underscores the need for greater consistency and transparency in research methodology to facilitate robust pooled analyses. Moreover, while this meta-analysis was able to examine changes over time for pain outcomes, similar long-term analyses for amputation, ulcer recurrence, and balance were not feasible due to a limited number of studies that reported outcomes at multiple intervals.

CONCLUSION

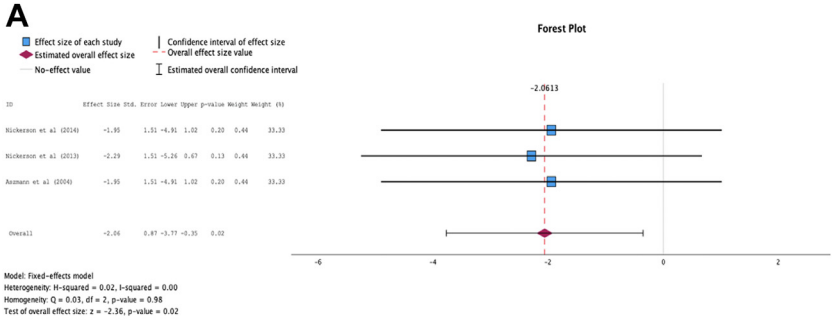
This comprehensive systematic review and meta-analysis demonstrate that surgical nerve decompression provides significant and sustained pain relief in patients with DPN, with benefits observed across short-term, medium-term, and long-term follow-up periods. Additionally, the intervention is associated with notable reductions in ulcer recurrence and lower-limb amputations, underscoring its potential to mitigate some of the most debilitating complications of DPN. Although improvements in sensory recovery are evident in analyses of continuous data and uncontrolled categorical studies, controlled comparisons did not consistently confirm these benefits. Furthermore, while a positive trend in balance improvement was observed, the limited data and methodological heterogeneity preclude definitive conclusions. Overall, our findings support the role of surgical decompression as a valuable therapeutic option for selected DPN patients. Future research should prioritize large-scale, rigorously designed RCTs employing standardized outcome measures to further elucidate the long-term benefits, optimize patient selection, and refine surgical techniques in this challenging population.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the authors used chatGPT in order to paraphrase. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

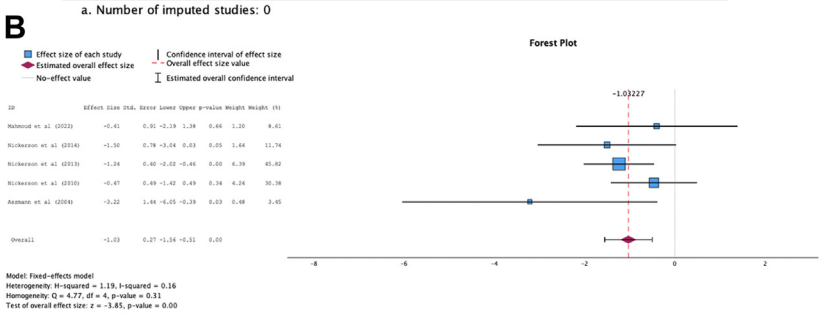
Shahin Naghizadeh: Writing — review & editing, Writing — original draft,



Effect Size Estimates for Trim-and-Fill Analysis

	Number	Effect Size	Std. Error	Z	Sig. (2-tailed)	95% Confidence Interval Lower	Upper
Observed	3	-2.061	.8729	-2.362	.018	-3.772	-.351
Observed + Imputed[a]	3	-2.061	.8729	-2.362	.018	-3.772	-.351

a. Number of imputed studies: 0



Effect Size Estimates for Trim-and-Fill Analysis

	Number	Effect Size	Std. Error	Z	Sig. (2-tailed)	95% Confidence Interval Lower	Upper
Observed	5	-1.032	.2678	-3.854	<.001	-1.557	-.507
Observed + Imputed[a]	5	-1.032	.2678	-3.854	<.001	-1.557	-.507

a. Number of imputed studies: 0

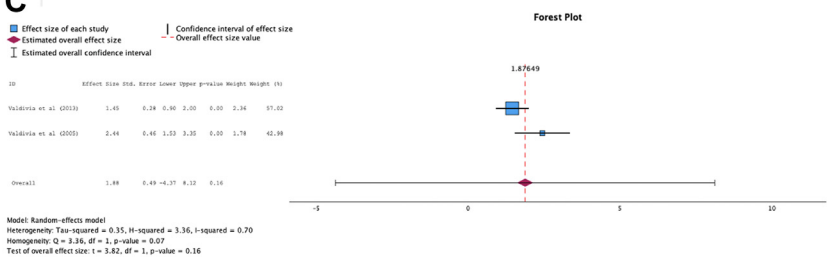


Figure 5. The forest plot and trim-and-fill analysis results (**A**) for amputations, (**B**) for ulcer recurrence, and (**C**) for balance improvement. The forest plot, showing the effect size and 95% confidence intervals for individual studies and the overall pooled estimate, and the trim-and-fill analysis results, demonstrating the robustness of the pooled estimate and addressing potential publication bias, for balance improvement; the regression-based test cannot be computed when the number of studies is less than or equal to 3.

Software, Methodology, Investigation, Formal analysis, Data curation. **Maryam Zohrabi-Fard:** Writing — review & editing, Software, Investigation, Formal analysis, Data curation. **Amir-Ahmad Keramati:** Writing — review & editing, Methodology, Investigation, Formal analysis, Data curation. **Alireza Zali:** Validation, Supervision. **Kaveh Oraii Yazdani:** Software, Project administration, Formal analysis. **Sadra Rohani:** Writing — review & editing, Methodology. **Saeed Oraee-Yazdani:** Writing — review & editing, Visualization, Validation, Supervision, Conceptualization.

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